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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/246,129	02/08/99	YU G	PF141P4

EXAMINER	
ROMEO, D	
ART UNIT	PAPER NUMBER
1647	15

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DATE MAILED: 03/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/246,129	Applicant(s) Yu et al.
	Examiner David Romeo	Group Art Unit 1647

☒ Responsive to communication(s) filed on *16 Jan 2001*.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *41-94* is/are pending in the application.

Of the above, claim(s) *41* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *42 and 49-94* is/are rejected.

☒ Claim(s) *43-48* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *13*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The amendment filed 01/16/2001 (Paper No. 14) has been entered. Claims 41-94 are pending. Claim 41 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6. Claims 42-94 are being examined.

2. The corrected or substitute drawings were received on 01/16/2001 (Paper No. 11). These drawings are acceptable.

3. Any objection and/or rejection of record that is not maintained and/or repeated in this Office action is withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

4. Claims 42, 49-94 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 2, 2 to 174 of SEQ ID NO: 2, and 28 to 174 of SEQ ID NO: 2, does not reasonably provide enablement for the other embodiments encompassed by

the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. See the Office action mailed 07/13/2000 (Paper No. 8) at paragraph 4.

Applicants' arguments have been fully considered but they are not persuasive.

The claims require that the polypeptide or fragment "binds an antibody specific for TNF-γ-α". The instant specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "TNF-γ-α". An artisan cannot determine what additional limitations are placed upon a claim by the presence of this term. The claims require an artisan to make through extensive, random, trial and error experimentation a "TNF-γ-α" polypeptide of unknown structure and unpredictable function and to determine through extensive, random, trial and error experimentation if antibodies to a "TNF-γ-α" polypeptide of unknown structure and unpredictable function bind either to a claimed polypeptide or to a fragment of a claimed polypeptide. The specification exemplifies a single species of the claimed invention. The claims do not even require that the antibody binding be to this single exemplified species. The claims only require that the antibody bind to a "TNF-γ-α" polypeptide of unknown structure and unpredictable function. It is also entirely unclear how an antibody that is specific for a genus of "TNF-γ-α" polypeptides of unknown structure and unpredictable function binds specifically to a "TNF-γ-α" polypeptide because binding to a genus of polypeptides implies binding to more than one polypeptide, and, hence, non-specificity. Other than SEQ ID NO: 2, the specification does

not provide guidance for which polypeptide in the genus of "TNF-γ-α" polypeptides of unknown structure and unpredictable function binds antibodies that also bind SEQ ID NO: 2. Furthermore, the claims do not appear to require that same specificity of interaction between the antibodies and a "TNF-γ-α" polypeptide of unknown structure and unpredictable function and a claimed polypeptide or fragment because the claims require that the antibody specifically bind a "TNF-γ-α" polypeptide of unknown structure and unpredictable function and bind a claimed polypeptide or fragment. Mere binding is tolerant of entirely nonspecific binding.

Claims that require a polypeptide or fragment have "TNF-γ-α activity" do not correspond in scope to the enabling disclosure because "TNF-γ-α activity" encompasses any and all conceivable activities, including those that are not described in the instant specification, whereas the specification only provides for the inhibition of angiogenesis. The specification does not limit "TNF-γ-α activity" to inhibition of angiogenesis, nor does it describe any and all uses encompassed by the term "TNF-γ-α activity". Absent a disclosure of uses for the polypeptides commensurate in scope with the term "TNF-γ-α activity", the disclosure manifestly fails to meet the "how to use" requirement of 35 U.S.C. § 112, first paragraph.

Claims that require a polypeptide comprising a fragment of an amino acid sequence wherein the fragment has "TNF-γ-α activity" or wherein the polypeptide or fragment is functionally unlimited only set forth a portion of the exemplified polypeptide and the structure of the claimed polypeptide is unlimited beyond that fragment. In the case where the polypeptide is

unlimited functionally, use of fragments of the exemplified polypeptide to elicit antibodies specific for the exemplified polypeptide does not extend to polypeptides which are tolerant as asserted of the presence of additional immunogenic sequences which may or may not be related to the exemplified polypeptide. The skilled artisan would not employ a polypeptide containing an unlimited plurality of unrelated epitopes to make antibodies specific for the exemplified polypeptide, nor would the artisan employ such polypeptides for related purposes, e.g. specific detection of the presence of antibodies to the exemplified polypeptide. Absent a disclosure of activities for the polypeptides commensurate in scope with the term "TNF-γ-α activity", the disclosure manifestly fails to teach "how to make" a fragment having "TNF-γ-α activity" and fails to teach "how to make" a polypeptide having "TNF-γ-α activity" from a fragment of the exemplified polypeptide.

In the case of a polypeptide having a recited % identity with SEQ ID NO: 2 wherein the polypeptide is functionally unlimited the specification has not told the skilled artisan how to use a polypeptide that does not have a specific activity instantly disclosed or has an activity that is not disclosed, unknown, and unpredictable. The claims are substantially broader than the species disclosed because the ability to be bound by specific antibodies does not correlate with retention of "TNF-γ-α activity" as one skilled in the art would fully appreciate and the specification does not disclose with any particularity the nature of "TNF-γ-α activity". The claimed functional genera encompassed by the term "TNF-γ-α activity" is represented in the disclosure by SEQ ID

NO: 2, 2 to 174 of SEQ ID NO: 2, and 28 to 174 of SEQ ID NO: 2. The claims do not require the essential features which permit the polypeptides they embrace to be used in a manner commensurate with the disclosure.

The claims also require a polypeptide with or without a functional limitation encoded by a nucleic acid molecule that hybridizes to a polynucleotide encoding SEQ ID NO: 2. A certain degree of similarity at the nucleotide level does not imply like similarity at the amino acid level because the claims embrace polypeptides encoded by truncation and frameshift variants, including those having no structural relationship to the exemplified TNF-γ-α. Furthermore, the disclosure provides no guidance as to which regions of the protein would be tolerant of modification and which would not, and it provides no working example of a variant sequence which would be within the claims. It is in no way predictable that randomly selected mutations, deletions, etc. in the disclosed sequence would afford a protein having activity comparable to the one disclosed.

Conclusion

5. Claims 43-48 are objected to as being dependent upon a rejected base claim.

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (703) 305-4050. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 6:45 A.M. TO 3:15 P.M.

IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, GARY KUNZ, CAN BE REACHED ON (703) 308-4623.

OFFICIAL PAPERS FILED BY FAX SHOULD BE DIRECTED TO (703) 308-4242.

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (703) 308-0294.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

MARCH 25, 2001